UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 10/573,385 | 05/07/2007 | Tomoki Hamamoto | 2006_0434A | 9339 |

513 7590 07/08/2009

WENDEROTH, LIND & PONACK, L.L.P.
1030 15th Street, N.W.,
Suite 400 East
Washington, DC 20005-1503

| EXAMINER | |
|---|---|
| EPPS -SMITH, JANET L | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1633 | |

| MAIL DATE | DELIVERY MODE |
|---|---|
| 07/08/2009 | PAPER |

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/573,385 | HAMAMOTO ET AL. | |
| | Examiner | Art Unit | |
| | Janet L. Epps-Smith | 1633 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *07 May 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-10* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *4-01-08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

### *Claim Rejections - 35 USC § 102*

1. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

2. Claim 1-2, 4-5 and 8 are rejected under 35 U.S.C. 102(b) as being anticipated by Simon et al. (JACS, 1988, Vol. 110, pages 7159-7163, see IDS).

Claim 1 recites the following:

1. (Original) A process for producing highly pure CMP-N-acetylneuraminic acid (CMP-NeuAc), comprising the following steps (1) to (4):
step (1): a step of adding a divalent cationic species to a CMP-NeuAc-containing solution, thereby causing phosphoric acid, pyrophosphoric acid, and a nucleotide which coexist with CMP-NeuAc to precipitate;
step (2): a step of adding a phosphatase to the CMP-NeuAc-containing solution, thereby converting the nucleotide which coexists with CMP-NeuAc into a nucleoside;
step (3): a step of adding an organic solvent, thereby precipitating CMP-NeuAc in the form of salt; and
step (4): a step of collecting the thus-precipitated CMP-NeuAc,
wherein these steps are performed in a predetermined combination.

Page 7162 teaches the following:

"**Purification of CMP-NeuAc: Differential Precipitation**. CMP-NeuAc was generated as described above except that the NeuAc (I g) Used had been purified by ion-exchange chromatography. The following steps were performed at 4 °C. The reaction mixture was centrifuged (25000g, 20 rain), and the pellet was resuspended in I00 mL of I0 mM NH4OH and centrifuged again. This wash procedure was repeated. Combination of the washings and dialysates (see above) yielded a solution whose pH was adjusted to pH 9.5 and was then concentrated; the pH must be checked when the volume is approximately halved and adjusted up to pH 9 during this step to prevent hydrolysis. The concentrate was desalted on Biogel P-2 (100 × 4.5 cm; eluant, 10 mM NH4OH), and the fractions containing CMP-NeuAc (determined by TLC as above) were pooled and concentrated to 30 mL. Slow addition of ethanol (30 mL) precipitated CT15, and the solution was centrifuged (10000g, 10 min). The supernatant containing CMP-

NeuAc was decanted, and the pellet was; resuspended in 30 mL of 10 mM NH4OH. The precipitation and centrifugation steps were repeated. The combined supernatants were concentrated to near dryness and redissolved in 50 mL of I0 mM NH4OH. The pH of the solution was adjusted to pH 9, and ***alkaline phosphatase (~200 U) and MgCl2.6H20 (1.1 g) was added as above.*** After 90 win, the pH of the solution was adjusted to 9.5 and the solution was centrifuged (10000g, 10 min). The supernatant was saved, the pellet was resuspended in25 mL of 10 mM NH4OH, and the solution was centrifuged again. This wash procedure was repeated. The combined supernatants were concentrated to~30 mL, and the addition of ***ethanol*** (270 mL) precipitated 5. The supernatant was concentrated to 30 mL, and the ***precipitation was repeated.*** The collected precipitates were desalted on Biogel P-2 as above to yield 1.2 g of a solid containing ~90% CMP-NeuAc (~50% yield from 2); pyruvate, dipyruvate, and an unidentified contaminant were also present."

Simon et al. also teach the following at page 7161:

**Isolation of CMP-NeuAc.** We found that the best way to separate CMP-NeuAc from CTP, PEP, CMP, cytidine, pyruvate, dipyruvate, Glc-NAc, phosphate, and inorganic salts was by ion-exchange chromatography using the formate form of anion exchange resin (AG 1-X2). The column was eluted with a gradient of aqueous ammonium bicarbonate. The use of ammonium bicarbonate prevented hydrolysis of acid-labile CMP-NeuAc and provided it as the ammonium salt. Excess ammonium bicarbonate was easily removed by stirring the fractions containing CMPNeuAc with *cation-exchange resin* (Dowex 50W-X8, H+ form) until the pH of the solution was **7.** To make the separation easier, residual nucleotides and excess PEP were hydrolyzed by using alkaline phosphatase before chromatography. The purity of CMP-NeuAc was >95%.

The method of Simon et al. clearly encompasses a method for purifying CMP-N-NeuAc wherein the method comprises the steps of (1) adding a divalent cationic species, namely MgCl2, (2) adding a phosphatase to the CMP-N-NeuAc solution, (3) adding an organic solvent, ethanol and (4) Collecting the precipitated CMP-NeuAc, (5) steps (3)-(4) are repeated.

## *Claim Rejections - 35 USC § 103*

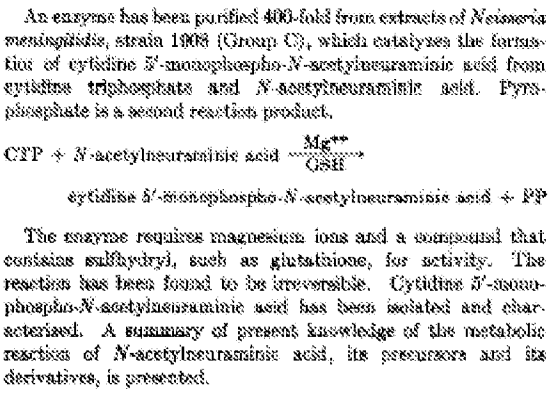
3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. Claims 1-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Simon et al. in view of Warren et al. and Vann et al.

The discussion of Simon et al. as set forth above is incorporated here. However, Simon et al. does not teach wherein the reaction mixture for the isolation of CMP-NeuAc comprises wherein the divalent cation species is calcium or manganese ion. Furthermore, Simon et al. does not teach a process according to claim 1, wherein these steps are performed in the following sequence: step (2), step (1), step (3), and then step (4).

Warren et al. teach the following:



An enzyme has been purified 400-fold from extracts of *Neisseria meningitidis*, strain 1908 (Group C), which catalyses the formation of cytidine 5'-monophospho-*N*-acetylneuraminic acid from cytidine triphosphate and *N*-acetylneuraminic acid. Pyrophosphate is a second reaction product.

$$\text{CTP} + \textit{N}\text{-acetylneuraminic acid} \xrightarrow[\text{GSH}]{Mg^{++}} \text{cytidine 5'-monophospho-}\textit{N}\text{-acetylneuraminic acid} + \text{PP}$$

The enzyme requires magnesium ions and a compound that contains sulfhydryl, such as glutathione, for activity. The reaction has been found to be irreversible. Cytidine 5'-monophospho-*N*-acetylneuraminic acid has been isolated and characterized. A summary of present knowledge of the metabolic reactions of *N*-acetylneuraminic acid, its precursors and its derivatives, is presented.

Vann et al. teach that N-acetylneuraminic acid cytidyltranferase catalyzes the formation of CMP-NeuAc, and that this enzyme has a requirement for $Mg^{+2}$ or $Mn^{+2}$.

It would have been obvious to the ordinary skilled artisan at the time of the instant invention to modify the teachings of Simon et al. in view of Warren et al. and Vann et al. in the design of the instant invention. One of ordinary skill in the art would have been motivated to make this modification since the prior art clearly teaches that the enzyme that catalyzes the formation of CMP-NeuAc requires a divalent cation for

activity, and further wherein the divalent cation includes manganese ion. Additionally, it would have been obvious to substitute one equivalent divalent cation (see that process of Simon et al. utilizes $MgCl_2$) for another (i.e. or $Mn^{+2}$) as taught by Vann et al., with the expectation of producing a similar result. See MPEP § 2144.06[R-6]II. SUBSTITUTING EQUIVALENTS KNOWN FOR THE SAME PURPOSE.

Moreover, in regards to claim 3, wherein the steps in the process for isolating pure CMP-NeuAc are performed in the following sequence: step (2), step (1), step (3), and then step (4) as defined in claim 1, absent evidence to the contrary it would have been obvious to the ordinary skill artisan to vary the parameters of a prior art method in an effort to optimize the results of the method. Regarding the rationale for combining prior art elements according to known methods to yield predictable results, all of the claimed elements were known in the prior art and one skilled in the art could have combined the element as claimed by known methods with no change in their respective functions, and the combination would have yielded predictable results to one of ordinary skill in the art at the time of the invention.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Janet L. Epps-Smith whose telephone number is 571-272-0757. The examiner can normally be reached on M-F, 10:00 AM through 6:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on 571-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Janet L. Epps-Smith/
Primary Examiner, Art Unit 1633